CHAPTER 3

Disinfection By-Product (DBP) Chemistry: Formation and Determination[1]

Introduction
The Need for Disinfection

In the mid 19th century, Chinese workers on the North American transcontinental railroad suffered less illness than other groups. While generally mysterious at the time, today the reason is obvious. The Chinese preference for tea required heating the water, thus killing many of the pathogenic microorganisms. Today, the need to kill microorganisms in water is largely met through the addition of oxidizing chemicals to the source water. The incidence of waterborne illness has decreased dramatically during the 20th century, increasing human productivity and longevity. In addition to affecting the microorganisms, however, the chemicals added to disinfect the water react with nonliving substances that occur naturally in drinking water sources. These disinfection by-products (DBPs), some of which are carcinogenic, are the subject of human health concerns.

While the basic chemistry of disinfectants outlined in this chapter has been fairly well understood for some time, the past 20 years have seen an incredible volume of scientific investigation into DBPs resulting from the use of these substances. At the beginning of the 1980s, a great majority of the work on DBPs was focused on the trihalomethanes (THMs), and much of it was performed by U.S. Environmental Protection Agency (EPA) Drinking Water Research facilities in support of the development of regulation. As interest in the potential health effects of disinfection has dramatically increased, EPA's direct contribution has become a smaller and smaller fraction of the work with each passing year. This reflects not a lack of interest or effort on the part of EPA, but the growth in interest outside the Agency. A perusal of university graduate schools shows the creation of environmental engineering departments as well as divisions of environmental chemistry through this time period. EPA Offices solicit and fund much research using contracts, cooperative agreements, and other vehicles. Most of the funding of unsolicited research proposals is performed by the EPA Office of Research and Development's (ORD) National Center for Environmental Research (NCER). The American Water Works Association Research Foundation (AWWARF) is a research organization dedicated to the needs of water utilities and, thanks to funding from EPA and AWWA members, has produced many results related to water utility operation and disinfection practice.

This chapter addresses some of the major issues in DBP formation chemistry, but focuses mostly on EPA-sponsored or in-house research. In addition to studies that attempt to qualitatively identify by-products, drinking water professionals have tried to understand the conditions that lead to the formation of DBPs and how these compounds are formed. In terms of monitoring and studying DBPs, it is clear that monitoring DBP formation requires appropriate analytical tools. To meet this need, an entire field of analytical chemistry has sprung up to support the study of DBP formation and regulation in potable water.

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Overview of Disinfection Issues

In the U.S., disinfection of drinking water is a common practice, although the choice of disinfectant varies. These disinfectants have in common an ability to inactivate microorganisms. The disinfectants destroy certain microscopic biochemical features of microorganisms, rendering them harmless to human health. Research into chemical treatment technologies has focused on individual disinfectants, although combinations of these disinfectants are often used. Table 3-1 lists the number of water supplies in the U.S. by the type of disinfectants used. Attributes of these disinfectants will be discussed in more detail in following sections of this chapter.

Table 3-1. Survey of Disinfectant Use (1997)

Type of Disinfectant	Number of Systems
Chlorine	22,307
Chlorine dioxide	313
Chloramines	135
Ozone	30
Potassium permanganate	1,122

The data in Table 3-1 are taken from a survey of disinfection practices published in 1997 (USEPA 1997). Of the disinfectants in Table 3-1, the use of ozone is increasing quickly, with 264 plants using ozone as of May 1998 (Rice et al. 1998), primarily as a response to the regulatory requirements discussed in more detail in Chapter 2.

Table 3-2 lists some of the microorganisms targeted by disinfection practice and some of the more appropriate disinfectants for each microorganism.

Table 3-2. Microorganisms and Disinfectants That Inactivate Them

Organism	Chemical Disinfectant	Health Effects
Bacteria such as *Legionella* and coliform *(Escherichia coli)*	Chlorine Chloramine Chlorine dioxide Ozone	Gastroenteric disease, Legionnaire's disease, death
Giardia lamblia cysts	Chlorine Chlorine dioxide Ozone	Gastroenteric disease, death
Cryptosporidium parvum oocysts	Chlorine dioxide Ozone	Gastroenteric disease, death
Viruses	Chlorine Chlorine dioxide Ozone	Gastroenteric disease, death

Like many technological improvements, disinfection has a downside. Namely, the disinfectants are often so powerful that they nonselectively react with other substances in the water to form what are known as DBPs. There are three classes of DBPs listed in Table 3-3, which also lists the residual disinfectants, i.e., the forms of the disinfectant left in the water. There are actually thousands of DBPs, and Table 3-3 lists some of the more common, more studied, and representative types. Some of the detailed studies are discussed in following sections. The health effects of some of the compounds listed in Table 3-3 (USEPA 1999a) have been investigated. Table 3-4 summarizes these health effects in accordance with the classification scheme described by Table 3-5. Note that EPA is in the process of revising the Cancer Guidelines (USEPA 1996) .

Table 3-3. List of DBPs and Disinfection Residuals

Disinfectant Residuals	Halogenated Organic By-Products
Free chlorine	Trihalomethanes
Hypochlorous acid	Chloroform
Hypochlorite ion	Bromodichloromethane
Chloramines	Dibromochloromethane
Monochloramine	Bromoform
Chlorine dioxide	Haloacetic acids[b]
Inorganic By-Products	Monochloroacetic acid
Chlorate ion	Dichloroacetic acid
Chlorite ion	Trichloroacetic acid
Bromate ion	Monobromoacetic acid
Organic Oxygenated By-Products	Dibromoacetic acid
Aldehydes[a]	Haloacetonitriles
Formaldehyde (methanal)	Dichloroacetonitrile
Acetaldehyde (ethanal)	Bromochloroacetonitrile
Glyoxal (ethanedial)	Dibromoacetonitrile
Pyruvaldehyde (oxopropanal)	Trichloroacetonitrile
Other aliphatic aldehydes	Haloketones
Carboxylic acids	1,1-Dichloropropanone
Acetic acid	1,1,1-Trichloropropanone
Other aliphatic monocarboxylic acids	Chlorophenols
Oxalic (ethanedioic) acid	2-Chlorophenol
Ketoacids[a, b]	2,4-Dichlorophenol
Glyoxylic (oxoethanoic) acid	2,4,6-Trichlorophenol
Pyruvic (oxopropanoic) acid	Chloropicrin
Ketomalonic (oxopropanedioic) acid	Chloral hydrate
Assimilable organic carbon	Cyanogen chloride
	Organic chloramines
	MX (3-Chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone)

[a] These carbonyl compounds are actually present as geminal diols even though their concentrations are reported in terms of the parent carbonyl compounds. See Urbansky 2000h for further explanation.
[b] Although reported as acids, these species are actually present in water as the deprotonated anions.

Table 3-4. Status of Health Information for Disinfectants and DBPs

Contaminant	Cancer Classification
Chloroform	B2
Bromodichloromethane	B2
Dibromochloromethane	C
Bromoform	B2
Monochloroacetic acid	–
Dichloroacetic acid	B2
Trichloroacetic acid	C
Dichloroacetonitrile	C
Bromochloroacetonitrile	–
Dibromoacetonitrile	C
Trichloroacetonitrile	–
1,1-Dichloropropanone	–
1,1,1-Trichloropropanone	–
2-Chlorophenol	D
2,4-Dichlorophenol	D
2,4,6-Trichlorophenol	B2
Chloropicrin	–
Chloral hydrate	C
Cyanogen chloride	–
Formaldehyde	B1[a]
Chlorate	–
Chlorite	D
Bromate	B2
Hypochlorous acid	–
Hypochlorite	–
Monochloramine	–
Chlorine dioxide	D

[a] Based on inhalation exposure.

Table 3-5. Scheme for Categorizing Chemicals According to Carcinogenic Potential

Group	Classification	Definition
A	Human carcinogen	Sufficient evidence in epidemiologic studies to support causal association between exposure and cancer.
B	Probable human carcinogen	Limited evidence in epidemiologic studies (Group B1) and/or sufficient evidence from animal studies (Group B2)
C	Possible human carcinogen	Limited evidence from animal studies and inadequate or no data in humans
D	Not classifiable	Inadequate or no human animal evidence of carcinogenicity
E	No evidence of human carcinogenicity	No evidence of carcinogenicity in at least two adequate animal tests in different species or in adequate epidemiologic and animal studies

Because of concern over these DBPs over the past 25 years, some DBPs have been regulated and/or subject to monitoring rules aimed at meeting the simultaneous goal of disinfecting water and controlling DBPs (USEPA 1999b). Table 3-6 lists these compounds along with important information about them. It is important to remember that Table 3-6 is a small subset of Table 3-3, which itself is a subset of the much larger list of substances sometimes identified as DBPs.

Regulatory issues were covered in more detail in Chapter 2, and a discussion of the Stage 1 DBP Rule explains how the costs and benefits were utilized to determine appropriate risk/exposure reduction (Roberson et al. 1995). From a scientific standpoint, in chlorinated potable water supplies, two classes of DBPs dominate the identifiable organic matter, the THMs and the haloacetates (haloacetic acids or

Table 3-6. National Primary Drinking Water Regulations Establishing Maximum Contaminant Levels (MCLs) and Maximum Contaminant Level Goals (MCLGs) Related to DBPs

Compound	MCLG (mg/L)	MCL (mg/L)	Potential Health Effects	Sources of Drinking Water Contamination
Bromate	Zero[a]	0.010[b]	Cancer	Ozonation by-product
Bromodichloromethane	Zero[b]	see TTHMs	Cancer, liver, kidney, reproductive effects	Drinking water chlorination and chloramination by-product
Bromoform	Zero[a]	see TTHMs	Cancer, nervous system, liver, kidney effects	Drinking water ozonation, chloramination, and chlorination by-product
Chlorite	0.8[a]	1.0[b]	Hemolytic anemia	Chlorine dioxide disinfection by-product
Chloroform	Zero[a]	see TTHMs	Cancer, liver, kidney, reproductive effects	Drinking water chlorination and chloramination by-product
Dibromochloromethane	0.06[a]	see TTHMs	Nervous system, liver, kidney, reproductive effects	Drinking water chlorination and chloramination by-product
Dichloroacetic acid	Zero[a]	see HAA5	Cancer and other effects	Drinking water chlorination and chloramination by-product
Haloacetic acids[c] (HAA5)	N/A	0.060[b]	Cancer and other effects	Drinking water chlorination and chloramination by-product
Trichloroacetic acid	0.3[a]	see HAA5	Possibly cancer and reproductive effects	Drinking water chlorination and chloramination by-product
Total trihalomethanes[d] (TTHMs)	N/A	0.08[b]	Cancer and other effects	Drinking water chlorination and chloramination by-product

Source: 63 *Federal Register* 69390

[a] Finalized on December 16, 1998 (63 *Federal Register* 69390) as established in 40 CFR 141.53.

[b] Finalized on December 16, 1998 (63 *Federal Register* 69390) as established in 40 CFR 141.64.

[c] HAA5 is the sum of the concentrations of mono-,di-, and trichloroacetic acids and mono- and dibromoacetic acids expressed in mg/L.

[d] Total Trihalomethanes are the sum of the concentrations of bromodichloromethane, dibromochloromethane, bromoform, and chloroform expressed in mg/L.

HAAs) and hence are of regulatory interest. In Table 3-7, the THMs are a group of compounds with three halogen atoms. Only the brominated and chlorinated ones are routinely found in potable water. Occasionally, iodinated products are found, and fluorinated ones do not occur naturally and are not formed during disinfection. The THMs are formed when individual carbon atoms are attacked by halogen disinfectants. Small hydrocarbon chains are cleaved from natural organic matter (NOM) mol-

ecules, and the reaction of the halogen species continues until THMs are formed. Small amounts of tetrahalomethanes (carbon tetrahalides) are also formed in this fashion; however, THMs account for some 20% of the halogenated organic carbon found after disinfection (Weinberg 1999).

Table 3-7. Trihalomethanes (THMs) Found in Potable Water

Name	Formula
Trichloromethane (chloroform)	$CHCl_3$
Bromodichloromethane	$CHBrCl_2$
Dibromochloromethane	$CHBr_2Cl$
Tribromomethane (bromoform)	$CHBr_3$

HAAs are also formed during chlorination. These DBPs are listed in Table 3-8. Like the THMs, the HAAs are also linked with increased incidence of cancer in laboratory animals (Xu et al. 1995; Herren-Freund et al. 1987). Unlike the THMs, the HAAs are capable of dissociating in water. HAAs are >99% ionized (deprotonated) to the haloacetate anions under drinking water conditions. However, they are regulated and usually reported in terms of the parent acids rather than the carboxylate anions. HAAs account for about 13% of the halogenated organic matter after disinfection (Weinberg 1999).

Table 3-8. Haloacetic acids (HAAs) Found in Potable Water

HAA	Formula	Grouping[a]
Chloroacetic	$ClCH_2CO_2H$	HAA5,6,9
Dichloroacetic	Cl_2CHCO_2H	HAA5,6,9
Trichloroacetic	Cl_3CCO_2H	HAA5,6,9
Bromoacetic	$BrCH_2CO_2H$	HAA5,6,9
Dibromoacetic	Br_2CHCO_2H	HAA5,6,9
Tribromoacetic	Br_3CCO_2H	HAA9
Bromochloroacetic	$BrClCHCO_2H$	HAA6,9
Bromodichloroacetic	$BrCl_2CCO_2H$	HAA9
Dibromochloroacetic	Br_2ClCCO_2H	HAA9

[a] HAA5 concentrations (as the sum) are regulated under the Stage 1 DBP Rule. HAA6 data must be obtained and reported under the Information Collection Rule (ICR). HAA9 data are encouraged to be obtained and reported under the ICR, but not required.

Of the DBPs listed in Table 3-3, bromate is formed from the ozonation of source waters which contain bromide. In ozonated water supplies, a variety of aldehydes and ketones abound as well as some carboxylic acids. In addition to these organic products, inorganic species are also found. These include oxyanions of halogens, such as chlorite, chlorate, and bromate, which can be formed by a variety of oxidizing disinfectants. Bromate is of particular interest since it is suspected of posing one of the highest cancer risks of any DBP.

General Issues in Disinfection: Disinfectants and Source Material for DBPs

Many excellent reviews have been written (White 1999; USEPA 1999a) about the general chemistry of the disinfectants in Table 3-1. The following sections discuss just a few of the relevant points of each. The source material, with which the disinfectant may react to form DBPs, is also briefly discussed.

Disinfectants that Contain Chlorine: General Chemistry
Chlorine: Chlorine(I) and Chlorine(0) Compounds

Chlorine is the most widely used disinfectant in the U.S. It is U.S. practice that finished drinking water leaves the treatment plant with a residual disinfectant. When surface water is used as the source for drinking water, residual disinfectant is required by regulation. Therefore, chlorine is often added to finished water, even if a different oxidant is used for primary disinfection. Chlorine is added to water in a variety of forms, usually as a gas or in the solid hypochlorite form.

Chlorine Gas

Chlorine gas, properly referred to as dichlorine (Cl_2), is a greenish yellow gas that has a familiar and pungent smell. Chlorine (oxidation state: 0) is modestly soluble in water. When added to water, chlorine hydrolyzes, producing hypochlorous and hydrochloric acids:

$$Cl_2 + H_2O \rightleftharpoons HOCl + Cl^- + H^+ \tag{3-1}$$

Hydrochloric acid is a strong acid and is completely dissociated into hydrogen and chloride ions. Hypochlorous acid (HOCl, chlorine oxidation state: +I) is a weak acid with a pK_a of about 7.5, and it dissociates into hydrogen and hypochlorite (OCl^-) ions:

$$HOCl \rightleftharpoons H^+ + OCl^- \tag{3-2}$$

It is believed that chlorine(0) and chlorine(I) compounds work primarily by denaturing enzymes or proteins, thereby inactivating microorganisms. In some cases, physical disruption of cell membranes may also contribute. HOCl is thought to be the more active species.

Hypochlorite

The equilibrium in Equation 3-1 can be driven forwards using strong base to deprotonate the hypochlorous acid and to neutralize the hydrogen ion:

$$Cl_2 + 2\ OH^- \rightleftharpoons OCl^- + Cl^- + H_2O \tag{3-3}$$

When sodium hydroxide is used as the base, the familiar sodium hypochlorite, found in household bleach, is formed, which in turn undergoes the following reaction:

$$NaOCl + H_2O \rightleftharpoons HOCl + Na^+ + OH^- \tag{3-4}$$
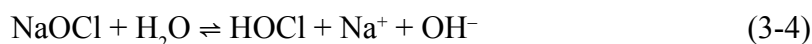
Thus, the same active species, HOCl, is produced from both the reaction of chlorine gas and solid hypochlorite.

Hypochlorous acid may also be produced by addition of solid calcium hypochlorite salt to water. The choice of using chlorine gas or hypochlorite salts is a matter of preference by water utilities and is often dictated by cost, safety concerns, and the availability of raw materials. The chemistry of chlorine has practical considerations in this regard: The chlorine(I)-cation transfer step means that chlorine and hypochlorous acid both undergo 2-electron reductions. If a reducing agent cannot offer 2 electrons, reactions are generally slow or difficult. The 2-electron reduction can be expressed as follows:

$$HOCl + H^+ + 2e^- \rightleftharpoons Cl^- + H_2O \tag{3-5}$$

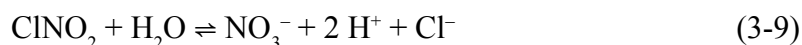$$Cl_2 + 2e^- \rightleftharpoons 2Cl^- \tag{3-6}$$
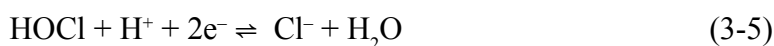
Chlorine(I) is unstable and disproportionates; thus, hypochlorite solutions are slowly converted to chlorate and chloride, which are not disinfection by-products in the sense that no other reactant is required:

$$3 \text{ ClO}^- \rightleftharpoons 2 \text{ Cl}^- + \text{ClO}_3^- \tag{3-7}$$

Given enough time, solutions of sodium hypochlorite (e.g., chlorine laundry bleach) will be more than 99% converted to chlorate and chloride. Equilibrium is achieved faster at higher temperatures. Chlorate is not a good disinfectant. Although the central chlorine atom has a high oxidation state (+V), chlorate reacts much more slowly than hypochlorite and only in acidic conditions, which, in turn, reacts more slowly than hypochlorous acid. This kinetic barrier precludes its use as an oxidizing disinfectant. Unlike hypochlorous acid, which reacts primarily by chlorine(I) cation transfers, chlorate must react either by a reductant attacking the central chlorine atom or an oxygen atom transfer. Hypochlorite loss via Equation 3-7 requires that a fresh supply of sodium hypochlorite solutions be available. As a rule, most chlorination plants dissolve the chlorine in a small amount of water just before adding it to the main stream, or they add the chlorine gas directly to the stream. Nonetheless, chlorate has been found in these disinfection solutions (Bolyard et al. 1992; Bolyard et al. 1993). By contrast, Cl_2 gas is stable indefinitely if stored properly.

Chlorine Reaction with Inorganic Material

Chlorine and hypochlorous acid (or hypochlorite) react not only with organic matter, but with a number of inorganic anions as well. In this way, a number of inorganic by-products are also produced. Chlorine(0) and chlorine(I) oxidize primarily by chlorine(I)-cation transfer. Although a net oxygen atom transfer occurs, many reactions proceed through the chlorine(I) transfer, followed by hydrolysis. For example, nitrite is oxidized to nitrate as follows:

$$\text{NO}_2^- + \text{HOCl} \rightleftharpoons \text{ClNO}_2 + \text{OH}^- \tag{3-8}$$

$$\text{ClNO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{NO}_3^- + 2 \text{ H}^+ + \text{Cl}^- \tag{3-9}$$

One beneficial reaction may occur when arsenic compounds, namely arsenite (As(III)), are present in the source water. Reaction with chlorine oxidizes arsenite to arsenate, As(V), which is easier to remove from the source water and is less toxic than arsenite:
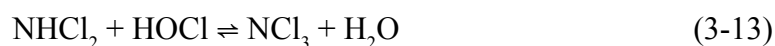
$$\text{As(III)} + \text{chlorine} \rightleftharpoons \text{As(V)} \tag{3-10}$$

Chloramines

Another chlorine-containing disinfectant is chloramine, which is formed from the reaction of ammonia with hypochlorous acid.

$$\text{NH}_3 + \text{HOCl} \rightleftharpoons \text{NH}_2\text{Cl} + \text{H}_2\text{O} \tag{3-11}$$

The addition of the ammonia (NH_3) ties up the "free" chlorine, available as HOCl. It also slows down undesirable reactions of "free" chlorine which form DBPs. The chemistry of chloramines becomes more complicated as shown in the following equations, in which the chloramine reacts with more hypochlorous acid to tie up more chlorine.

$$\text{NH}_2\text{Cl} + \text{HOCl} \rightleftharpoons \text{NHCl}_2 + \text{H}_2\text{O} \tag{3-12}$$

$$\text{NHCl}_2 + \text{HOCl} \rightleftharpoons \text{NCl}_3 + \text{H}_2\text{O} \tag{3-13}$$
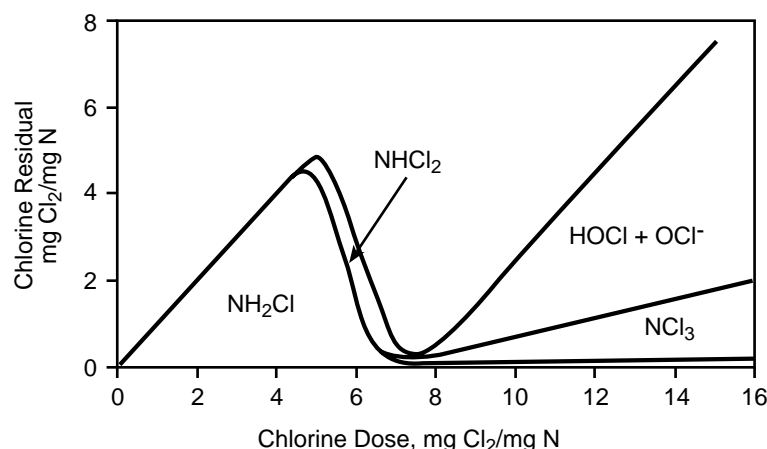
Figure 3-1. Speciation of free and combined chlorine species. When ammonia and chlorine are reacted at various ratios, different concentrations of mono-, di-, and trichloramine are formed. At Cl$_2$/N (w/w) ratio of about 7, breakthrough occurs, producing NCl$_3$, which is not useful as a disinfectant.

Together, the chloramines are referred to as combined chlorine. The equilibrium for the three reactions, Equations 3-11 to 3-13, produces the distribution of species shown in Figure 3-1.

Figure 3-1 illustrates that, above a particular chlorine dose, the chlorine residual—and disinfection ability—goes down almost to zero. In other words, the chlorine dose must be carefully controlled to maintain a chlorine residual. If sufficient chlorine is added, another phenomenon known as breakpoint chlorination occurs. In breakpoint chlorination, the nitrogen(–III) in ammonaceous (organic) and ammoniacal (inorganic) species is oxidized to nitrogen(0). Superchlorination (shock treatment) of swimming pools takes advantage of this phenomenon after organic amines and ammonia build up over the winter. In addition, the equilibrium is quite sensitive to the pH. Coupled with the breakthrough phenomenon, the operation of chloramine plants can be complicated because the pH and chlorine dose must be carefully controlled. However, if used properly, chloramination is a tool for DBP control.

Chlorine Dioxide: a Chlorine(IV) Compound

The various oxidation states of chlorine make it useful in other disinfectants, such as chlorine dioxide (ClO$_2$), which is very much unlike chlorine and hypochlorous acid. This unusual oxide contains chlorine in the +IV oxidation state. It is a moderately stable radical, ClO$_2\bullet$, which does not undergo further reaction with water after it dissolves. The mechanism by which chlorine dioxide reacts with most other species is believed to be a mixture of oxygen atom-transfer and electron-transfer steps. This allows single-electron reductions along with multiple-electron pathway transfers:

$$ClO_2(aq) + e^- \rightleftharpoons ClO_2^- \tag{3-14}$$

$$ClO_2^- + 2\ H_2O + 4e^- \rightleftharpoons Cl^- + 4OH^- \tag{3-15}$$

$$ClO_3^- + H_2O + 2e^- \rightleftharpoons ClO_2^- + 2OH^- \tag{3-16}$$

$$ClO_3^- + 2H^+ + e^- \rightleftharpoons ClO_2^- + H_2O \tag{3-17}$$

Equations 3-14 to 3-17 illustrate how both chlorite (ClO$_2^-$) and chlorate (ClO$_3^-$) can be produced as a result of the use of chlorine dioxide.

Disinfectants Not Containing Chlorine: General Chemistry
Potassium Permanganate

Nonchlorine-containing disinfectants require another species to act as oxidizing agent. In terms of disinfection, this usually requires oxygen-containing species that are powerful enough to disrupt the functioning of the microorganism. Potassium permanganate, $KMnO_4$, is a weaker oxidant. It is used mostly for iron and manganese removal, or taste and odor control, but can lower the level of DBP precursor material. The reduction of Mn^{VII} (oxidation state: +VII) to Mn^{IV} (oxidation state: +IV) provides the oxidation ability via the following half-reactions:

$$MnO_4^- + 4H^+ + 3e^- \rightleftharpoons MnO_2 + 2H_2O \qquad (3\text{-}18)$$

$$MnO_4^- + 8H^+ + 5e^- \rightleftharpoons Mn^{2+} + 4H_2O \qquad (3\text{-}19)$$

$$MnO_4^- + 2H_2O + 3e^- \rightleftharpoons MnO_2 + 4OH^- \qquad (3\text{-}20)$$

These reactions can oxidize some organic and inorganic DBP source material and inactivate some microorganisms, but are not powerful enough to inactivate many bacteria and protozoa. When used in conjunction with another oxidant, such as chlorine, potassium permanganate can be advantageous because it has already oxidized some DBP source material. Thus, DBPs are controlled. If used improperly, the residual permanganate anion renders the water pink. Potassium permanganate is a well-understood system and is not the subject of much research investigation, as the by-products are regarded as innocuous.

Ozone

Like chlorine dioxide, ozone (O_3) must be generated on site. However, this process is fairly straightforward and less susceptible to problems than chlorine dioxide. Ozone is generated by passing an electrical discharge through dioxygen (O_2):

$$3O_2(g) \rightleftharpoons 2O_3(g) \qquad (3\text{-}21)$$

Figure 3-2. Scheme showing the production of bromate in ozonated systems.

Ozone is responsible for the familiar smell associated with lightning strikes. Ozone is a powerful oxidant which engages in oxygen atom transfers. In addition to the direct action of O_3 on living tissue, ozone can cleave water molecules, producing hydroxyl radical (OH•), which also can act as a disinfectant. The contribution of each of the dual pathways, direct ozone and indirect hydroxyl, is highly dependent on the source water quality because various chemicals, such as the ubiquitous carbonate, tend to deactivate the hydroxyl pathways. The reaction of ozone with the bromide ion is important in DBP formation, and its complexities are illustrated in Figure 3-2.

Ozone and hydroxyl radical attack a variety of sites in organic molecules. Of particular interest is the fact that ozone is far more effective than hypochlorite or chlorine for inactivating *Cryptosporidium* oocysts. At the concentrations normally used for disinfecting drinking water, chlorination does not affect cryptosporidians significantly, but ozone does. The reaction of ozone has a tendency to produce many oxygenated compounds, such as carboxylic acids, aldehydes, and ketones, which are nutritious compounds for microorganisms.

An Overview of Disinfection By-Product Formation Source Material

The source material for DBPs is important in understanding the chemistry and mechanism of DBP formation, once the disinfectant reacts with the source material. Other chapters in this book deal with the removal of this material to prevent DBP formation, and other facets of DBP/microbial issues relate to the presence of source material.

Inorganic Sources

Source material for the formation of DBPs is inorganic and organic in nature. Inorganic components are traced to various minerals and other substances in the water derived from nonbiological sources. These substances occur naturally in the water or may be anthropogenic in nature. One such naturally occurring substance is the anion known as bromide, which is implicated in by-product formation, particularly when used with ozone. Bromide in the water can also contribute, through a series of reactions, to brominated products when chlorine is used. Bromide contamination in chlorine solutions is another route through which bromide enters drinking water.

Natural Organic Matter (NOM)

Natural waters used as sources for drinking water supplies contain a variety of types of organic matter. Some of this organic matter comes from natural sources. When organisms die, a mixture of biological and chemical processes take place. These processes produce a mixture of compounds that are collectively referred to as NOM. NOM can be highly variable, depending on its source and extent of degradation. Many factors besides native flora and fauna influence NOM composition. These include temperature, rainfall/humidity, light, microbial populations, and geography. There is a complex interplay among the native flora and fauna as well as the climate and season. There is much interest in understanding the makeup of this material. The International Humic Substances Society (http://www.ihss.gatech.edu), for instance, comprises scientists interested in NOM.

A variety of schemes have been used to classify NOM. These categories are not mutually exclusive. One of the oldest and most respected (albeit generalized) methods is based on the solubility under different pH conditions. Humic acid is the fraction of NOM in water not soluble at pH < 2, but soluble at higher pH. Fulvic acid is soluble at all pHs. Humin is not soluble at any pH. When describing the conjugate bases (e.g., the sodium salts), the terms humate and fulvate, respectively, are used.

Characterization of NOM

Typical soluble NOM has a molecular mass range of about 300 to 30,000 unified atomic mass units (or daltons, Da). Common moieties include aromatic rings, alkyl chains, carboxylates, phenols, and other alcohols. Polynuclear (polycyclic) aromatic compounds are not generally thought of as making up a significant portion of NOM. A number of volumes have been dedicated to characterizing NOM (AWWA 1994; Barret and Krasner 2000; Minear and Amy 1996a; Owen et al. 1993; Croue et al. 1999).

Because NOM does not reflect a single compound or even a closely related group of compounds, it is very difficult to characterize. Therefore, NOM is sometimes fractionated based on its physical properties, such as polarity, namely its relative retention on functionalized poly(styrene-divinylbenzene) resins (e.g., Rohm & Haas XAD®). Other physical properties, such as ionizability, are also used. The U.S. Geological Survey has developed elaborate techniques to fractionate NOM and characterize the individual fractions. EPA currently is involved in multiple cooperative efforts to relate NOM characteristics to DBP formation.

Aside from fractionation, another avenue of NOM characterization is to study properties of the bulk solution rather than individual chemical components. As a bulk source of organic carbon, NOM is often measured in raw and finished water using total organic carbon (TOC) analyzers (Urbansky 2001). Modern TOC analyzers convert the carbon in organic carbon compounds to carbon dioxide, which is then measured with an infrared detector. In addition to TOC, which includes suspended particulate matter, dissolved organic carbon (DOC) can also be reported. In practice, DOC is most often used, and most TOC analyzers are more effective at determining DOC than TOC.

Techniques commonly used for characterization rely on identifying individual functional groups, such as amines, thiols, alcohols, carboxylates, and halides. In addition, NOM can be subjected to traditional elemental analysis by combustion. Infrared spectroscopy is one of the instrumental techniques that can assess some of the functional groups present since certain moieties are known to have distinct infrared absorption bands that correspond to O-H stretch, C=O stretch, or other types of independent vibrations. Nuclear magnetic resonance (NMR) spectroscopy is used to distinguish among aromatic, alkyl, and alkenyl compounds. Relative contributions of these different types of carbon-carbon bonds can be estimated from the NMR spectra. Pyrolysis-GC/MS can fingerprint NOM in terms of four biopolymer groupings, namely, polysaccharides, proteins, aminosugars, and polyhydroxyaromatic compounds. The complexity of the sample can produce difficulties in interpretation for whatever technique is used.

Factors Affecting DBP Formation from the Source Material

A number of factors in addition to the NOM composition determine the composition of DBPs. The choice of oxidizing disinfectant is an obvious factor. The presence of other ions, such as bromide, can have a profound impact on the nature and distribution of the DBPs formed during water treatment. Temperature, pH, and oxidant dosing rates all can affect DBP formation. Hundreds or perhaps thousands of papers have been written on small variations in conditions that affect DBP formation. A whole series, Water Chlorination Volumes 1–6, edited by R.L. Jolley (Jolley 1976; Jolley et al. 1978, 1980, 1983, 1985, 1990) was dedicated to water chlorination chemistry. Several recent volumes have continued down this path (Symons 1997; Minear and Amy 1996b; Singer 1999).

More effort is focused on removing DBP precursors (i.e., NOM) (Shorney and Freeman 1999). Many of EPA's surface water treatment rules emphasize this approach. The Stage 1 DBP Rule considers this to be an important aspect because it is neither possible nor practical to identify or monitor the plethora of by-products that form during disinfection with oxidizing compounds. Certain classes of compounds are monitored, but, to account for the many that cannot be, minimizing the amount of precursor material is adjudged to be one of the best approaches.

EPA Research into DBP Formation and Chemistry
Measures of the Proclivity of NOM To Form DBPs

By definition, NOM is a reducing agent. When an oxidant, such as chlorine or hypochlorous acid, is exposed to NOM, a variety of oxidation-reduction reactions is possible. Every natural water has an oxidant demand. For example, when chlorine is used, the chlorine demand is a measure of the ability of dissolved organic matter to react with chlorine. Until the chlorine demand is satisfied, disinfection is a compromise between the oxidant reacting with the NOM and the microorganism, so disinfection efficiency decreases. Once the chlorine demand is satisfied (essentially everything that can react with chlorine has), additional chlorine goes to disinfection. As far as DBP formation is concerned, the chlorine demand in and of itself is not a measure of the tendency to form DBPs. Much of the chlorine added to meet demand is reduced entirely to chloride rather than being incorporated into a halogenated by-product.

To have some quantitative measure of the proclivity of NOM to form DBPs, a test for the THM formation potential or THMFP has been devised. The formation potential is determined by exposing a raw (untreated) water sample to an excess of oxidizing disinfectant for a period of time at a specific temperature. The change in THM concentration relative to time zero is the THMFP. The total concentration of THMs at any time is expressible as

$$[CHX_3]_T = [CHCl_3] + [CHBrCl_2] + [CHBr_2Cl] + [CHBr_3] \qquad (3\text{-}22)$$

Thus, the THMFP(a) at time $t = a$ is given by

$$THMFP(a) = [CHX_3]_T(t = a) - [CHX_3]_T(t = 0) \qquad (3\text{-}23)$$

In practice, a quantity of oxidant is added to a fixed volume of water and an aliquot is drawn out at defined time intervals. This aliquot is then analyzed to determine the concentrations of THMs in solution. The THMFP, expressed in concentration units, is an estimate of the maximal concentration of DBPs that may be formed in the presence of a large excess of oxidant. One of the problems with the way the THMFP has been applied is that the measurement conditions were not the same in different investigations. This makes it difficult to compare or contrast the values obtained. In order to standardize the THMFP, a set of *uniform formation conditions* (UFC) has been developed (Summers et al. 1996) under EPA sponsorship. These can be summarized as follows: pH = 8.0 ± 0.2 (borate buffer), temperature = 20 ± 1°C, reaction time = 24 ± 1 hr, and active chlorine residual = 1.0 ± 0.4 mg L^{-1} as Cl$_2$ (28 µM), which is representative of routine operating conditions. On the other hand, if a sample of finished water with a typical chlorine residual is monitored for THM concentration as a function of time, this simulates the behavior of the water once it leaves the utility plant and makes its way into the distribution system on its way to consumers. This procedure is referred to as a simulated distribution system (SDS) THM test. In this case, it is possible for all the chlorine to be consumed, unlike the THMFP test. Depending on the location, consumption rate, and water pipe size, treated or finished water may linger for days in the distribution system.

Chlorination By-Products
Halogenation of NOM

Halogenated (brominated and/or chlorinated) compounds are of greatest concern due to health effects observed in laboratory animals. Total organic halide (TOX), a concept largely developed/promoted by EPA (Stevens 1984) is defined as the sum of the concentrations of all halogenated organic compounds. The true value of the TOX concentration cannot be determined; the number and identities of the indi-

vidual halogenated compounds formed during disinfection are unknown. Therefore, in practice, the TOX concentration is operationally defined with measurement by a TOX analyzer. TOX analyzers use activated carbon to capture halogenated organic matter. The carbon is then combusted at about 800-1000°C to convert all halogens to the hydrohalic acids (HX). The halide ion is then coulometrically titrated with silver(I) and expressed as chloride. Halogenated organic matter that is not readily or strongly adsorbed to activated carbon is routinely lost, negatively biasing the reported TOX value. Compounds other than THMs and HAAs, such as 2,2,2-trichloroethanediol (chloral hydrate), haloacetonitriles, or trichloronitromethane (chloropicrin), can also be found in chlorinated potable water supplies. Together, the haloacetonitriles make up about 2% of the halogenated organic matter, and 2,2,2-trichloroethanediol also makes up about 2% of the halogenated organic matter after disinfection takes place (Weinberg 1999). These DBP species form regardless of the source of the NOM. It is believed that the same types of structures are responsible for DBP formation on a molecular level. These structures are thought to be duplicated throughtout NOM molecules regardless of the overall size of the molecule. This results in fairly uniform distribution of baseline DBPs, such as THMs and HAAs when water is chlorinated. Other by-products can also be formed.

Much of EPA's initial research focused directly on characterizing and exposing NOM to oxidizing disinfectants, especially active chlorine compounds. In this way, EPA identified a number of classes of compounds that make up NOM and established procedures for extracting DBPs from solution using XAD® resins (Christman et al. 1980, 1983b). Because algae can be found growing in finished water reservoirs, concern over plant metabolic products led to studies in that area. Extracellular products resulting from algal growth were shown to react with chlorine, forming chloroform in addition to higher-molecular-mass (>1000 u) DBPs (Wachter and Andelman 1984). A number of chlorinated DBPs were determined from the reaction with several NOM sources, including surface water and commercial products isolated from soils (Seeger et al. 1984b, 1984b). XAD® resins were used to collect the DBPs, which were eluted with ethyl ether. Many chlorinated aromatic carboxylic acids were found by gas chromatography-mass spectrometry (GC/MS), including some with ether linkages. Oxygenated DBPs were also found, including some longer-chain carboxylic acids (Seeger et al. 1984a, 1984b). As should be expected, chlorination of amino acids produced halonitriles; what was unexpected, perhaps, was the formation of high levels of 2,2,2-trichloroethanediol (Trehy et al. 1986). Chlorination of NOM isolated from a lake in North Carolina was demonstrated to produce a number of short-chain chlorinated carboxylic acids, including haloacetic acids and some alkenyl species in addition to THMs and 2,2,2-trichloroethanediol (Christman et al. 1983a). A variety of mutagenic compounds, including THMs, HAAs, haloacetonitriles, and haloketones were demonstrated to form when NOM is chlorinated directly (Meier et al. 1985). The mutagenicity of some HAAs was demonstrated by EPA (Meier et al. 1997). Accounting for the post-disinfection halogenated organic matter has been continually problematic. In general, studies have accounted for no more than 60% of the halogenated organic matter measured as TOX, and sometimes as little as 15% (Norwood et al. 1983). NOM was characterized by ^{13}C NMR to distinguish between aliphatic and aromatic portions as well as ultraviolet (UV) spectrophotometry (Reckhow et al. 1990). Chlorination of the NOM gave a mixture of DBPs, including several HAAs and haloacetonitriles. This study also attempted to link the various measurable characteristics of the NOM (humate and fulvate) to the distribution of DBPs. Another study (Fromme et al. 1995) marginally linked the presence of biopolymeric groups quantitated by pyrolysis GC/MS with DBP formation.

Other Sources of DBP Precursors

In addition to natural sources of NOM, anthropogenic (man-made) sources of organic matter exist, too. For example, water treatment chemicals were shown to be a source of organic matter that led to the

formation of DBPs (Feige et al. 1980). The release of industrial chemicals and minerals is largely an unknown contributor to DBP formation. In this case, the type of DBPs is highly site specific. Regulated DBPs, on the other hand, tend to be formed regardless of source water.

Foodstuffs and, indeed, bodily fluids can also potentially be DBP precursors, considering that a quantity of disinfectants are ingested. Because most tap water contains a chlorine residual, it is possible for DBPs to form even after the water is consumed. As a model, when rats consumed sodium hypochlorite (albeit at levels higher than would normally be found in potable water), THMs, HAAs, and haloacetonitriles were detected in both the gastric contents and the plasma (Mink et al. 1983). Oxidizing chlorine compounds can react with a variety of natural compounds, including carboxylic acids found in fruit juices. Such reactions have been shown to produce mutagenic organic compounds (Chang et al. 1988). A recent study demonstrated that foods and beverages could provide an alternate exposure route to DBPs (Raymer et al. 1999a, 1999b).

Influences on and Mechanisms of DBP Formation

As noted earlier, a number of factors can influence DBP formation (Johnson et al. 1986). EPA has funded or specifically worked on several of these. A significant advance in measuring the proclivity for THM formation was the establishment of the uniform formation conditions (Summers et al. 1996). The location in the plant where chlorination occurs can affect DBP formation. Prechlorination is practiced by many utility plants to oxidize iron(II) and manganese(II) as well as to minimize biological growth in their agglutination-sedimentation facilities. However, agglutination-sedimentation removes a significant fraction of NOM. Accordingly, prechlorination has been demonstrated to lead to additional DBP formation (Solarik et al. 1997).

When waters contain bromide, chlorination produces a variety of brominated by-products. Bromide is oxidized by chlorine(I) to give bromine(I). At drinking water pH, most chlorine(I) is in the form of hypochlorite; however, hypobromite is a stronger base, and so the oxidation-reduction reaction is accompanied by hydrolysis:

$$ClO^- + Br^- + H_2O \rightarrow Cl^- + HOBr + OH^- \qquad (3\text{-}24)$$

HOBr is kinetically more labile than hypochlorous acid even though it is a weaker oxidant from a thermodynamic standpoint. Thus, bromination reactions abound during chlorination. In this fashion, a mixture of brominated, chlorinated, and bromochlorinated by-products are formed during disinfection. Studies have attempted to evaluate the effect of bromide on the formation of mutagenic by-products; for example, a study conducted with Jefferson Parish, LA, water considered the effect of bromide (Coleman et al. 1992). Chlorination of source water containing bromide results in the formation of not only chlorinated DBPs, but also brominated and bromochlorinated DBPs (Coleman et al. 1992). Other studies have identified some of these brominated, chlorinated, and bromochlorinated by-products (Caughran et al. 1999; Richardson et al. 1999a).

The precise quantities of the specific brominated, chlorinated, and bromochlorinated by-products requires further research. Some studies, however, have focused particularly on HAAs and THMs because they are known to make up much of the identifiable DBPs and are the subject of regulation. As pH goes down, the formation of brominated species increases (Pourmoghaddas et al. 1993; Pourmoghaddas 1991). This occurs because most reactions involving hypohalous acids proceed through a halogen(I) cation transfer step (Equation 3-25). This elementary reaction proceeds faster in acidic solutions because a hydroxide leaving group is more favorable than an oxide leaving group (which would have to be converted to hydroxide in water due to the leveling effect of the solvent).

$$RCH{=}CH_2 + HOBr \rightleftharpoons [RCH{-}CH_2Br]^+ + OH^- \qquad (3\text{-}25)*$$

* In this case, bromine is shown adding to the less-substituted carbon atom. Regioselectivity of these reactions is a complicated subject and beyond the scope of this work.

The tendency to form brominated versus chlorinated species is also dependent on the DBP precursor material (NOM). For example, some types of NOM tend to form brominated HAA species, while some types of NOM tend to form chlorinated species (Magnuson and Kelty 2000).

In addition to more fundamental studies of chemical kinetics, attempts have been made to empirically model DBP formation (Clark et al. 1996). Because NOM is an ill-defined material, it is not possible to elucidate rigorously detailed reaction mechanisms. To help water utilities comply with the surface water treatment rules and the disinfection by-product rules, the Office of Water has prepared a modeling program that can be used in conjunction with site-specific chemical and engineering data (USEPA 1992, 1994). More details on modeling developments may be found in Chapter 9.

Investigating DBPs with Genotoxicity Assays

The goal behind studying and regulating DBPs has been the protection of human health. There are several measures of the effect of DBPs on human health. Some DBPs have been studied extensively enough to be assigned a carcinogenicity rating (refer to Table 3-4). However, given the large number of DBPs, many of which have not been identified, it has not been practical or economically possible to study them all. Therefore, other measures of potential human health effects have been explored. One of these is genotoxicity, which is a measure of the ability of a substance to damage the genetic material of an organism. The Ames Salmonella mutagenicity assay, which detects point mutations, is one of the most commonly used short-term tests for genotoxicity. It has been used extensively to detect the presence of genotoxicity in drinking water sample concentrates. There is substantial evidence that most of mutagenic activity in drinking water originates from the reaction of disinfectants, especially chlorine, with the NOM present in source waters (Meier 1988). Because of the formation of mutagenic compounds during disinfection, the Ames Salmonella assay has been used extensively to determine the levels of mutagenicity in finished water concentrates from both chlorinated (Schenck Patterson and Lykins 1993; DeMarini et al. 1995) and alternative disinfectants (Schenck Patterson and Lykins 1995; Schenck Patterson et al. 1995; DeMarini et al. 1995) as well as wastewaters (Meier and Bishop 1985; Doerger et al. 1992).

In addition to DBPs, source-specific contaminants from various industrial, agricultural, and municipal sources may also contribute to the overall mutagenicity of some drinking waters. Mutagenic contaminants could be introduced during distribution by such things as leaching of mutagenic materials from the inside of pipes or tanks. Also, openings in the distribution system may allow for the entry of contaminants from the outside. The level of mutagenicity in a drinking water may also increase within the distribution system, due to the continued formation of DBPs from the reaction of residual disinfectant with organic matter in the water.

Mutagenic compounds have been concentrated from finished water by reverse osmosis and then subjected to GC/MS (Coleman et al. 1980). GC/MS was originally used to identify and quantify about one-fourth of the TOX, including HAAs, haloacetonitriles, haloketones, and several other compounds (Coleman et al. 1984). GC/MS methods have been developed to measure mutagenic compounds in studies where NOM was chlorinated directly (Meier et al. 1983; Meier and Bull 1984; Meier et al. 1985a; Stevens et al. 1989). These studies are ultimately aimed at providing a model for the formation of mutagens during chlorination of actual drinking water, i.e., to predict which mutagenic DBPs are likely to be formed.
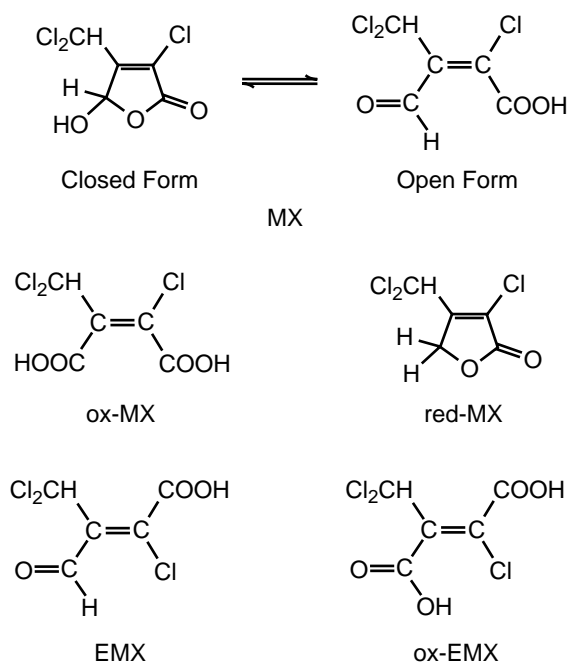
Figure 3-3. MX and its structural analogues (adapted from Richardson 1998a).

The discovery of the highly mutagenic compound, originally known only as Mutagen X (MX), prompted considerable research in potable water. The genotoxic and toxic properties of MX and related compounds have been reviewed elsewhere (Meier et al. 1990; Daniel et al. 1993). Many research papers were subsequently devoted to assaying this species. Other studies were carried out to determine the chemical properties of MX (Meier et al. 1987). MX is (*Z*)-2-chloro-3-(dichloromethyl)-4-oxobutenoic acid. It engages in a cyclization equilibrium to form a chlorinated furanone (*R,S*)-3-chloro-4-(dichloromethyl)-5-hydroxy-[5*H*]furan-2-one with the double bond still in the (*Z*)-configuration. Several chlorinated furanones, including MX, were shown to form when NOM was chlorinated directly (Meier et al. 1986). Figure 3-3 shows several of these forms. Despite small structural differences, MX is by far the most mutagenic compound.

MX and related mutagenic compounds can also form when NOM is chloraminated (Kanniganati et al. 1992). MX has been found in U.S. potable water supplies (Munch et al. 1988). It can be recovered from finished chlorinated water using XAD® resins (Schenck et al. 1990; Ringhand et al. 1988a, 1988b). Moreover, stability studies suggested that MX could survive in the distribution system for days (Meier et al. 1987).

Studies were made of MX and related compounds using GC with mass spectrometric and/or infrared spectrophotometric detection; these studies helped to identify these species in drinking water matrices (Collette et al. 1991). MX and related compounds have also been separated by liquid chromatography (Meier et al. 1986). The studies on MX were reviewed, outlining its chemical, mutagenic, and toxicological properties (Ringhand et al. 1989). Adverse effects on rats and mice were determined, but human effects were not clear (Daniel et al. 1994). Later, it was determined that MX was substantially detoxified in vivo in rats and that very little was excreted in the urine (Meier et al. 1996). In addition, risk was shown to be considerably lower than that from the THMs because of the level of exposure. Furthermore, the animal studies used concentrations about 1000 times greater than those found in chlorinated water (Melnick et al. 1997). Concentrations of MX in chlorinated water are in the low parts-per-trillion range. By contrast, THM levels in the same waters are typically 1000 times higher.

Trace DBPs in Drinking Water

Aside from the regulated DBPs, there are hundreds and perhaps thousands of other compounds formed from the reaction of disinfectant with substances in the water. In the strictest sense, products from the reaction between oxidizing disinfectants and either NOM or naturally occurring inorganic constituents are bona fide DBPs. On the other hand, some investigators classify all products formed from reactions with substances in the raw water regardless of source (e.g., anthropogenic chemicals, microorganisms, etc.) as DBPs. The observation of the plethora of chemicals formed was made early on, and much research went into trying to identify other DBPs, motivated by health concerns that trace levels may be problematic for chemicals such as MX or bromate. The problem is that mass spectrometry, a powerful method for identifying and quantifying DBPs, requires larger quantities of some DBPs than are naturally formed in drinking waters. Therefore, early research used concentrated solutions of NOM to increase the amount of DBPs formed and provided early evidence of the suspected link between NOM in water and DBP formation in drinking water (Kopfler et al. 1984). Likewise, a library of DBPs was built based on a natural water that contained an unusually high amount of NOM (Slocum et al. 1988). In this manner, a library of over 780 DBPs was developed (Stevens et al. 1987), with particular regard to the conditions required for formation. Because NOM differs greatly with source, later work was aimed at concentrating the DBP formed from large volumes of water. Several methods for concentrating the water were investigated and compared, and XAD® resins were determined to provide advantages over Grob closed loop stripping apparatus (CLSA) and purge and trap (Melton et al. 1981). XAD® was used to study 580 compounds in several water supplies (Lin et al. 1981). Although initially undertaken for mutagenicity studies, NOM extracts were subjected to mass spectrometry and other spectral techniques, resulting in the identification of hundreds of compounds (Richardson et al. 1994, 1996, 1999a, 1999b).

DBPs Formed from Alternative Disinfectants
DBP Formation from Alternative Disinfectants

Alternative disinfectants, namely disinfectants that are not chlorine gas or hypochlorite solutions, have been under study for some time in EPA, and they were the subject of an early review (Stevens and Symons 1984). The outside research community quickly picked up on DBP studies of alternative disinfectants. Within the EPA, the paradigm shift toward risk management (assessment and control) meant that more emphasis was placed on the risks associated with the consumption of water rather than the identification of all DBPs. To this end, several studies were performed to elucidate various issues that were relevant to this effort. One such issue involves ozone reaction pathways (ozone vs. hydroxyl), which are fundamental to understanding how to control the risks associated with ozone use, namely bromate formation. Hydroxyl radicals form during ozonation; a method was developed for rapidly measuring hydroxyl radical concentrations (Ireland and Velinieks 1992). The modeling of ozone/hydroxyl radical behavior and the effect on ozonation was studied, and the R_{ct} concept was described (Elovitz and von Gunten 2000), namely:

$$R_{ct} = [\text{OH} \bullet]/[\text{O}_3] \tag{3-26}$$

The formation of DBPs by these radicals was studied. In addition to ozonation, hydroxyl radicals are made when titanium dioxide is exposed to UV light, electrons are promoted in energy. This allows water to be cleaved to form hydroxyl radicals. Thus, a number of oxygenated DBPs were formed and later identified by multispectral analysis (Richardson et al. 1996).

Another research venture was preozonation, which, when coupled with chlorination, can be used to reduce DBP formation. The ozone breaks down the NOM into smaller molecules and leaves fewer of

the highly reactive sites; thus, the chlorine has fewer places to react (Miltner et al. 1992). Ozone can react with bromide to produce a variety of oxidized forms of bromine. These have been shown to react with NOM to make bromohydrins (Collette et al. 1994; Cavanagh et al. 1992). Bicarbonate can affect the efficacy of preozonation (Reckhow et al. 1986). Carbonate(1−) radical ($CO_3^-\bullet$) formed by the action of ozone on bicarbonate is a poor oxidant and would be expected to interfere in preozonation.

In order to better understand potential use of chloramine in reducing DBP formation, literature from the period 1946 to 1984 was reviewed for THM formation from chlorine and chloramine, including in the presence of bromide (Cooper et al. 1985). In summary, chloramine is a weaker oxidant than hypochlorous acid from a thermodynamic standpoint. For this reason, it usually results in lower levels of DBP formation, but it is not as good a disinfectant. The factors affecting DBP formation during chloramination have been studied (Symons et al. 1998; EPA 1989). Cyanogen chloride is one of the most recent chloramination by-products to be identified and studied; it can form when ozonated water is chloraminated (Pedersen et al. 1999). This compound can be formed from the reaction of chloramine and methanal (formaldehyde). The kinetics and mechanism of the reaction have been studied (Pedersen et al. 1999). Methanal is ubiquitous from natural processes, but it can also be formed by the reaction of hypochlorous acid with glycine, an amino acid that can be found in natural waters (Snyder and Margerum 1982).

DBP formation for chlorine dioxide was compared to that from ozone, chlorine, and chloramine (Koffskey 1993; Lykins et al. 1994). These studies found that no quick and easy conclusion could be reached regarding choice of disinfectant in terms of minimizing DBP formation, but that it was necessary to strike a balance among competing needs. Chlorate formation from chlorine dioxide disinfection was demonstrated when treated water is exposed to light, as is possible in coagulation-sedimentation basins (Bolyard et al. 1993).

Analytical Chemistry of Alternative DBPs

Several analytical methods have been developed for chloraminated water. Purge and trap GC/MS was used for cyanogen chloride analysis (Prakash et al. 1998), which compliments other methods of analysis of chloraminated water. Membrane introduction mass spectrometry was used to study the lifetime of monochloramine in the human body. Human saliva and stomach fluid were examined for monochloramine. Due to low time persistence, any toxic affects associated with chloramine were attributed to DBPs rather than the disinfectant (Kotiaho et al. 1992).

Ozonation by-products have been identified using many of the same techniques and methods that work for chlorination by-products (Richardson et al. 1999a, 1999b). EPA developed Method 556 to determine the aldehydes that form from ozonation (Munch et al. 1998a). The aldehydes make up a major fraction of ozonation by-products. This was followed by the preparation of a user's guide to help laboratories work around some known difficulties of the method (Munch et al. 1998b). Other by-products form, too, such as carboxylic acids, including a number of 2-oxocarboxylates, commonly referred to as ketoacids. A comparison of ion chromatography (IC) versus GC for the determination of the 2-oxocarboxylates showed that the ion chromatographic method was more rugged and less susceptible to problems during the analysis compared to the double derivatization/GC experiment described (Urbansky and Bashe 2000). The GC approach also suffered from interferences due to metal cations commonly found in water supplies (Urbansky 2000d). As with chlorination DBP formation studies, ozonation DBP studies also require the use of a reducing agent to eliminate residual oxidant. Problems with a variety of reagents were identified when applied to the determination of aldehydes (Urbansky et al. 2000a). It was later shown that indigo-5,5′,7-trisulfonate and triphenylphosphine could be used as fast-acting ozone-scavenging reagents (Urbansky et al. 2000b).

Many of the DBPs formed from ozonation experiments are highly polar in nature and therefore not amenable to many conventional forms of analysis. The difficulty is that water in which the DBPs are located is polar, and analytical techniques have difficulty separating the trace amounts of polar DBPs out of the far more numerous polar water molecules (Weinberg 1999). These compounds have been extracted from water through the use of solid phase microextraction (Shoemaker et al. 1999) or through the use of derivatizing agents, which convert the polar molecules into less polar ones, which are easier to extract. For example, aldehydes and ketones were analyzed following derivatization with 2,4-dinitrophenylhydrazine (Guo et al. 1998).

The use of spectroscopy techniques in addition to mass spectrometry has been used to help identify DBPs. One of these is infrared (IR) spectroscopy. This has been used in a number of studies with chlorine and non-chlorine disinfectants. For instance, multispectral analytical methods have been applied to determine DBPs in waters disinfected with chlorine and other disinfectants (Richardson et al. 1994, 1995, 1998a). Multispectral techniques have also been applied to identify aldehydes (Richardson et al. 1991). IR spectroscopy was a component of this multispectral analysis and is discussed in some detail separately (Collette 1996).

Analytical Methods Development for Regulated DBPs

Mass spectrometry allows the study of molecules by, to put it colloquially, weighing them. To be more precise, the mass/charge ration of ions resulting from the fragmentation of a molecule, as well as the fragmentation pattern, is determined accurately. Mass spectrometry has long been the dominant means to identify DBPs regardless of oxidizing agent. The quantification of DBPs through mass spectrometry as well as other detectors forms the basis of many EPA methods to monitor regulated DBPs.

Analytical method development has taken an important role in EPA/ORD DBP strategy, since in order to monitor, study, and regulate a DBP, a reliable method of analysis is necessary. Mass spectrometry is often the recommended technique to identify and/or quantify DBPs, although other detectors are permissible. The use of mass spectrometry, because it produces such a definitive result, has gone far in ensuring the quality of data generated from compliance monitoring and risk management studies. Ensuring the quality is essential if decisions are to be based on those data. EPA has helped to define practices for ensuring quality data (Budde and Eichelberger 1980; Boyd et al. 1996).

This effort has culminated in the development and promulgation of approved methods of analyzing DBPs in drinking water. Many of these methods can be used for determining regulated DBPs as well as unregulated DBPs, which is useful for fundamental studies of these compounds. Table 3-9 summarizes the methods for the regulated DBPs.

Table 3-9. EPA Methods for Regulatory Compliance Monitoring of Organic DBPs in Drinking Water

Method No.	Contaminant(s)
551	Halogenated hydrocarbons (including THMs), 2,2,2-trichloroethanediol, haloacetonitriles
502.2	THMs
524.2	THMs
552	HAA5 (see Table 2-2)
552.1	HAA5
552.2	HAA9
556	Aldehydes
300.x	Bromate, chlorite, chlorate
317.0	Bromate
321.8	Bromate

Trihalomethanes (THMs)

As shown by Table 3-9, there are often multiple methods for each DBP. Each method uses different techniques and equipment because some compliance monitoring laboratories may be skilled in one technique and/or may not have the equipment for another technique. Each method has been rigorously evaluated to meet the requirements for compliance monitoring. These techniques are revised and updated as new technology becomes available.

Closed loop stripping analysis, in which a large volume of water is effectively extracted into a small volume of carbon disulfide, was used when DBP studies were first initiated. The carbon disulfide would be injected into a gas chromatograph for detection with mass spectrometry or another suitable detector (Coleman et al. 1981). With the development of purge and trap technology by EPA, analysis of volatile DBPs was improved. Purge and trap methods are still effective and have been supplemented by liquid-liquid microextraction techniques. The analysis of drinking water developments from 1996 through 1998 has been recently reviewed (Richardson 1999), in which the EPA developed many methods that are not necessarily used in compliance monitoring, but are instead used for specific research purposes.

For the THMs, Methods 502.2 (Ho et al. 1995) and 524.2 (Eichelberger 1995) are based on purge and trap technology. In the purge and trap procedure, the water sample is placed in a specially designed vessel and an inert gas is bubbled through the water sample through a frit, which causes the bubbles to be small. The analytes (THMs) are purged by the inert gas and trapped on an adsorbent material. This adsorbent material is then heated rapidly to release the analytes. A gas chromatograph separates the mixture of analytes more or less by their volatilities and their abilities to partition into the stationary phase of the column. In Method 502.2, the analytes are detected by photoionization and electrolytic conductivity detectors. Detection is by elution time only and can be partially confirmed by the use of a dissimilar chromatography column. For more reliable identification, a mass spectrometer is used in Method 524.2.

Method 551.0 was designed originally for only DBPs, but was later expanded into Method 551.1 to determine a variety of pesticides and halogenated solvents encountered in drinking water (Hautman and Munch 1997). Method 551.1 (Munch and Hautman 1995) extracts the water sample with an organic liquid. The analytes (THMs) are more soluble in the organic liquid than they are in the water, so a portion of the analyte molecules partition into the organic liquid. This organic liquid is then injected into the gas chromatograph and is detected by an electron capture detector, which is very sensitive to the chlorine and bromine atoms in the analytes. Qualitative confirmation of the identity of the analyte is recommended by mass spectrometry.

Aside from these compliance monitoring regulatory methods, EPA has developed alternative methods to analyze THMs for special, i.e., research, purposes. For instance, to investigate more rapid analysis, THMs were purged directly into an electrolytic conductivity detector (Hodakievic and Ho 1990). Treatment studies often have special analytical needs that cannot be met using methods developed for regulatory compliance monitoring. In particular, DBP formation studies require that residual oxidants be quenched to fix the DBP concentrations in time. The EPA method specifies ammonium chloride or sodium sulfite. Recently, ascorbic acid has been used for this purpose for HAAs, haloacetonitriles, THMs, and other analytes of Methods 551.1A/B and 552.2 (Urbansky 1999; Urbansky et al. 2000c) as well as 502.2 analytes (Ho 1995). Bromochloroacetate possesses a chiral carbon atom; thus, some work has focused on determining the enantiomer ratios (Wong et al. 1999).

Haloacetic Acids (HAAs)

HAAs are more difficult to determine than THMs, and the analytical chemistry has been recently reviewed elsewhere (Urbansky 2000e). This is a result of the acidic nature of these contaminants, which causes them to not be amenable to direct GC analysis like the THMs. To solve this problem, EPA Method 552.0 (Hodgeson et al. 1988) provides for the analysis of 5 HAAs using diazomethane to esterify the analytes after extraction into *tert*-butyl methyl ether. The methyl esters are then injected into a GC and detected by electron capture. Advice for using this procedure was provided (Ulmer et al. 1988). Method 552.1 followed, replacing the diazomethane with acidified methanol. In Method 552.1, the analytes were extracted by running the tap water through a solid phase anion exchange resin. The current version of the method, Method 552.2 (Munch et al. 1995b), eliminates the use of explosive diazomethane, which is the most carcinogenic substance known to man (on a base pair methylation basis). Method 552.2 was designed with the preferred steps from both 552 and 552.1. Method 552.2 combines an MTBE extraction with acidified methanol esterification (Pawlecki-Vonderheide et al. 1997). Method 552.2 was verified for all 9 HAAs. Although EPA promulgated Method 552.2 to monitor HAA9 under the Information Collection Rule, many laboratories have continued to use Method 552. More care is necessary with Method 552 because diazomethane used in Method 552 degrades the brominated trihaloacetic acids, especially in white light (Rubio et al. 2000). Following the promulgation of the Information Collection Rule, EPA attempted to discern how well labs were doing using EPA-approved methods for DBP quantification (Stultz et al. 1998). The performance of Method 552.2 is dependent on both the specific water used and the skill of the analyst, particularly for the brominated trihaloacetic acids. As an alternative, complexation electrospray mass spectrometry was recently used to determine HAA9 in drinking water. Because it does not have the acidic methanol step, problems with the brominated trihaloacetic acids are reduced (Magnuson and Kelty 2000).

Inorganic DBPs: Bromate and Chlorite

Inorganic anions, e.g., bromate and chlorite, are produced as DBPs. They have been determined using ion chromatography originally developed in EPA Method 300.0 (Pfaff 1993). Bromate has attracted the most attention due to higher possible health risk. Several IC methods have been developed for this purpose (Hautman and Bolyard 1992a, 1992b, 1992c; Wagner et al. 1998). Lowering the detection limit has been the goal of this research. Several concentration techniques were proposed (Sorrell and Hautman 1993; Hautman 1993). EPA developed a method for bromate based on a chromophoric reaction; this lowered the detection limit substantially (Wagner et al. 1998), but the method can be affected by impurities in the 3,3-dimethoxybenzidine used as a prochromophore (Urbansky and Brown 2000). A GC/MS method has been developed for bromate; bromate is used to produce a volatile brominated organic molecule (Magnuson 1998). IC coupled with Inductively Coupled Plasma Mass Spectrometry (ICP-MS) has been extensively investigated to determine bromate in potable water under a variety of conditions (Creed et al. 1996, 1997a; Brockoff and Creed 1997). IC-ICP-MS is the basis of Method 321.8 (Creed et al. 1997b). Through the use of IC-ICP-MS, it was determined that brominated HAAs may interfere with the IC analysis of bromate (Creed et al. 1997a). Isotope dilution IC-ICP-MS was investigated for the determination of bromate (Creed and Brockhoff 1999). Isotope dilution involves adding a known amount of bromate labeled with a stable (non-radioactive) bromine isotope to the water sample before analysis. Whatever chemically and physically happens to the analyte (bromate) also happens to the isotopic addition. Therefore, isotopic addition is considered a primary and truly definitive form of measurement.

Directions in DBP Analytical Chemistry Research

Carcinogenicity has been the primary driving force behind drinking water regulations, and it is likely that carcinogenicity will continue in this role, although other health effects end points may also be of concern. Genotoxicity data, not limited just to mutagenicity assays, will probably continue to be used in assessing health risks of DBPs. However, relatively little effort has been paid to assessing other types of health effects, such as reproduction and sensitive populations (Bove et al. 1995; Waller et al. 1998). Reproductive end points are the subject of current EPA/ORD investigation, and the area of other end points for human health effects could be an interesting area of DBP research for the future. These end points may be associated with biologically active compounds that remain unidentified. Should a DBP be implicated in health risks associated with a form of disinfection, analytical methods will be needed for its analysis.

Another area of future DBP research is in the 60% or so of the halogenated material that is not part of the identifiable classes of compounds (i.e., HAAs, THMs, haloacetonitriles [HANs]). It is possible that some other highly active compounds are present, especially since the nonvolatile polar compounds are not well characterized. With the shift in the risk management paradigm, it is not known whether there will be large-scale continued interest in the identification of new DBPs. In the past, a large effort has been directed toward first identifying DBPs and then pursuing toxicology/pharmacokinetic studies. Unquestionably, this has been successful in encouraging utilities to use treatment practices capable of reducing the concentrations of several key DBPs, including the THMs and HAAs. Because the number of DBPs is essentially limitless due to the wide range of compounds that make up NOM, the feasability of large-scale DBP identification efforts is discussed (Urbansky 2000f) in light of more directed approaches towards specific human health goals. One such approach is the use of structure-activity relationships (SARs) (McKinney et al. 2000; Moudgal et al. 2000). SARs are based on the presumption that toxicity is not governed simply by the presence of a halogen, but rather that similar functional groups are responsible for the mechanisms of toxicity. There is no *a priori* basis for asserting that halogenated organic compounds are necessarily toxic; indeed, many halogenated organic compounds find use as pharmaceuticals. Likewise, advances in epidemiology and biostatistics can pinpoint human disease end points for further elucidation (Calderon 2000). Combining SARs with epidemiologic studies can focus the analytical chemistry on specific classes of compounds rather than expending time and resources on identifying benign spectator compounds.

New advances in analytical chemistry may complement the use of SARs, epidemiology, and biostatistics. DNA microarray technology permits rapid assessment of individual compounds or groups of compounds to evaluate not only additivity, but also synergy. These methods can be cheaper and faster than traditional animal toxicology/pathology studies, which consume considerable resources and require sacrificing many laboratory animals. Microarrays are currently being used to investigate DBPs and endocrine disruptors (Betts 2000). The National Institute of Environmental and Health Sciences (NIEHS) has created a Microarray Center to study and document genotypic changes (Cooney 2000). Like biological systems, these arrays can be exposed to complex mixtures in order to measure additive and synergistic effects. The arrays are already making headway in pharmaceutical and biotechnology research.

Research on compounds likely to adversely affect health can be further guided by judicious use of fractionated, but unidentified materials (Mount and Anderson-Carnahan 1988). If compounds are separated using chromatographic, electrophoretic, or other means, the individual fractions may be tested on microarrays, using indicator organisms (e.g., helminths, cladocerans, amphipods, insect naiads, or cope-

pods) that have well-known physiology, anatomy, and biology. Such organisms are routinely collected from natural waterways as ecological indicators of water quality, serving to identify the presence of pollutants. The advantage of using biological organisms is that additive effects can be observed even if the active principles exist at concentrations below the detection limits offered by modern analytical chemistry. Moreover, if the effects are synergistic rather than additive, a biological system can be used to observe the interaction phenomena in ways that no current chemoanalytical method could. The advantage of testing fractionated material before identifying its constituents is that chemicals in samples shown to be devoid of toxicity need not be identified at all. Consequently, these in vitro biotoxicity tests serve as a screening mechanism for weeding out countless harmless spectators, saving resources. This approach has been applied to estrogenic materials in sewage plant effluents and other mixtures more complex than finished drinking water (Desbrow et al. 1998).

From a practical standpoint, there are unresolved issues about how many DBPs reach the drinking water consumers. There are often lengthy delays in the water distribution system, and it is not always clear how DBP concentrations change after leaving the water plant and before the water reaches the tap. The stability of DBPs may be affected by reaction with components of the distribution, i.e., pipes, valves, tanks, etc. Kinetic studies of DBP chemistry under distribution system conditions may someday elucidate this. In the case of HAAs, for example, the concentration profiles observed in the distribution system show losses inconsistent with the known chemical kinetics (Urbansky 2000g). It has been speculated that biodegradation is responsible for this loss, but there are many unresolved issues, such as the potential for heterogeneous catalysis or homogeneous catalysis (general acid/base) (Urbansky 2000g).

From the standpoint of considering DBPs for regulation, research must consider whether existing regulations are already sufficient to control a candidate compound for regulation. Suppose that THM regulations require water treatment plants to be operated in such a manner that compound Y, a candidate for regulation, is controlled at the same time. Promulgating a regulation specifically for compound Y would then offer no additional benefit to public health. Accordingly, the expense associated with the development and support of such a regulation would not be warranted.

An additional direction for DBP research may be provided through extramural projects. While the primary focus of this chapter is research conducted or managed by EPA's research laboratories, EPA/ORD's National Center for Environmental Research continues to fund a wide range of research proposals in the area of disinfection by-products, as mentioned previously. For completeness, a list of recent and ongoing projects, along with the investigators' institutions, appears in Table 3-10.

Table 3-10. DBP Research Funded Through NCER

Title	Institution	Grant Number
Ion-Pair/Supercritical Fluid Extraction and Derivatization for Polar Organic Pollutant Analysis	Oregon State University	R821195
Novel Method for DBP Removal	Universal Fuel Development Associates, Inc.	68D50145
Development of a Novel Ferroelectric, Cathode-Based Ozonator for Drinking Water Treatment	UHV Technologies, Inc.	68D98149
A Comparison of the Effectiveness of Reverse Osmosis and Ion Exchange Technologies on the Removal of the Bromide Ion	University of Nevada, Reno	GF9501942
Investigation of Model Titania Surfaces for Heterogeneous Photocatalytic Oxidation of Chlorinated Organics	Arizona State University, Tempe	R819286
Development of Biomarkers for Haloacetonitriles-Induced Cell Injury in Peripheral Blood	The University of Texas Medical Branch, Galveston	R825955
Water Solubility and Henry's Law Constant	Lamar University	084LUB5101
Novel Method for DBP Precursor Removal	Universal Fuel Development Associates, Inc.	68D40043
Combined Ozonation and Biological Treatment for the Removal of Humic Substances from Drinking Waters	Michigan State University	GF9500518
Analysis of Organic By-Products from the Use of Ozone/Chlorine and Ozone/ Chloramines in Drinking Water Treatment	University of Massachusetts	R825364
Kinetic-Based Models for Bromate Formation in Natural Waters	Arizona State University	R826835
Use of Differential Spectroscopy to Probe Reactions between Natural Organic Matter and Chlorinated Oxidants	University of Washington, Seattle, WA	R826645
Engineering of Oxidation and Granular Activated Carbon Treatment Processes to Meet New Objectives in Drinking Water Treatment	University of North Carolina	R820184
Removal of Chlorine Dioxide By-Products from Drinking Water	Novatek	68D00033
Singlet Oxygen Disinfection of Drinking Water	Fayette Environmental Services, Inc.	68D99049
Zeolite Membranes for Removal of Contaminants in Drinking Water	TDA Research, Inc.	68D50081
Acoustic-Enhanced Ozone Drinking Water Disinfection	Montec Associates, Inc.	68D99059
The Particle Size Distribution of Toxicity in Metal-Contaminated Sediments	Colorado School of Mines, Colorado State University	R826651
Assessment of Human Dietary Ingestion Exposures to Water Disinfection By-Products via Food	Research Triangle Institute, NC	R826836

Title	Institution	Grant Number
Molecular Weight Separation and HPLC/MS/MS Characterization of Previously Unidentified Drinking Water Disinfection By-Products	University of Illinois at Urbana-Champaign and Metropolitan Water District of Southern California	R826834
Formation and Stability of Ozonation By-Products in Drinking Water	University of North Carolina at Chapel Hill	R826833
Mechanisms and Kinetics of Chloramine Loss and By-Product Formation in the Presence of Reactive Drinking Water Distribution System Constituents	University of Iowa	R826832
Mechanistic-Based Disinfectant and Disinfectant By-Product Models for Chlorine Decay and Regulated DBP Formation Derived from Free Chlorination	Arizona State University, University of Massachusetts, University of Colorado, Malcolm Pirnie	R826831
Integrated Approach for the Control of *Cryptosporidium parvum* Oocysts and Disinfection By-Products in Drinking Water Treated with Ozone and Chloramines	University of Illinois at Urbana-Champaign	R826830
Pilot Studies of the Ozonation/FBT Process for the Control of Disinfection By-Products in Drinking Water	Michigan State University	R826829
Inhalation and Dermal Exposure to Disinfection By-Products of Chlorinated Drinking Water	Environmental and Occupational Health Sciences Institute, University of Medicine and Dentistry of New Jersey	R825953
Development of a New, Simple, Innovative Procedure for the Analysis of Bromate and Other Oxy-Halides at Sub-ppb Levels in Drinking Water	University of North Carolina at Chapel Hill	R825952
Genotoxicity and Occurrence Assessment of Disinfection By-Product Mixtures in Drinking Water	University of Illinois at Urbana-Champaign	R825956
Metabolic Fate of Halogenated Disinfection By-Products In Vivo and Relation to Biological Activity	University of North Carolina at Chapel Hill	R825957
The Secondary Structure of Humic Acid and its Environmental Implications	University of Idaho	R822832
Fate of Bromate Ion and Bromine Compounds in Water Treatment	Purdue University	R821245

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